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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/597,920	06/19/2000	Lawrence E. Samelson	NIH-05065	4586

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Edwards & Angell LLP
PO Box 55874
Boston, MA 02205

EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n N .	Applicant(s)	
	09/597,920	SAMELSON ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears n the c ver sheet with the correspondence address --
Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 91-143 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 91-102 and 143 is/are allowed.
- 6) ☒ Claim(s) 103-142 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-90 have been canceled.
Claim 100 has been amended.
Claims 103-143 have been added.
2. Claims 91-143 are under examination.
3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.
4. The following Office Action contains NEW GROUNDS of rejection.

Rejections Withdrawn

5. The rejection of claims 81, 83-90 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.
6. The rejection of claims 85-87, 100 under 35 U.S.C. 112, first paragraph is withdrawn in view of the amendments to the claims.

Response to Arguments

7. The rejection of newly added claims 123, 132-139 under 35 U.S.C. 102(b) as being anticipated by Buday et al (The Journal of Biological Chemistry 269:9019-9023, 1994, IDS #5) and as evidenced from the specification is maintained.

The response filed 11/4/04 has been carefully considered but is deemed not to be persuasive. The response states that the antibody of Buday do not specifically bind to an amino acid sequence according to SEQ ID NO:4 but bind to many proteins and the antibodies are not generated against a polypeptide comprising at least about five non-phosphorylated amino acids or antibodies are not generated against a polypeptide comprising at least about five amino acids of SEQ ID NO:4 (see page 11-12 of response). In response to this argument, claims 123, 132-139 recite antibodies which are generated against at least five amino acids comprising a phosphotyrosine residue and as such the art of Buday reads on the claims because the antibody of Buday binds to anti-phosphotyrosine residues and as such the claim requires a phosphotyrosine residue and as long as the amino acids in the five amino acids have the phosphotyrosine as claimed then the antibody of Buday would bind. As far as the argument of "specifically binds" is concerned, this was addressed in the previous response, the specification does not define the phrase and as such the broadest interpretation is applied. In addition, applicants are directed to Roitt et al. (Immunology, third edition., Mosby, St. Louis, pages 6.4 and 6.5, 1993). Roitt teaches in the last sentence of the bridging paragraph of pages 6.4 and 6.5 that "when some of the determinants of an antigen, [for instance] A, are shared by another antigen, B, then a

Art Unit: 1642

proportion of the antibodies directed to A will also react with B. This phenomenon is termed cross-reactivity." See Fig 6.8 on page 6.4. Furthermore, specificity is not equivocal to exclusivity. Roitt continues to state on page 6.5, column 2, second paragraph, "The specificity of a population of antibodies is not due to each antibody reacting exclusively with the induction antigen." The rejection is maintained because Buday's antibody would be specific for SEQ ID NO:4. This is explained as follows, because the claims recite that the antibody is generated against a polypeptide comprising any 5 or 20 or residues 31-233 of SEQ ID NO:4 the antibody of Buday would recognizes the phosphotyrosine in SEQ ID NO:4 which can be generated against the entire protein (comprising) or any residues that contain the phosphotyrosine residue. If the entire protein was used as an immunogen or any fragment that has the phosphotyrosine residue, antibodies can be generated that bind the phosphotyrosine residue, such as Buday's. In addition, because the antigen is in 293T cells the antibody of Buday would bind. Also one would readily envisage that the antibody would not stain endothelial cells because the antigen is not found there. Thus, the art reads on the claims.

8. The rejection of newly added claims 123-131 under 35 U.S.C. 102(e) as being anticipated by Hirth et al (U.S. Patent 5,958,959, filed 6/1/95) is maintained.

The response filed 11/4/04 has been carefully considered but is deemed not to be persuasive. The response states that the antibody of Buday do not specifically bind to an amino acid sequence according to SEQ ID NO:4 but bind to many proteins and

Art Unit: 1642

the antibodies are not generated against a polypeptide comprising at least about five non-phosphorylated amino acids or antibodies are not generated against a polypeptide comprising at least about five amino acids of SEQ ID NO:4 (see page 11-12 of response). In response to this argument claims 123-131 recite antibodies which are generated against at least five amino acids comprising a phosphotyrosine residue and as such the art of Hirth reads on the claims because the antibody of Hirth binds to anti-phosphotyrosine residues and as such the claim requires a phosphotyrosine residue and as long as the amino acids in the five amino acids have the phosphotyrosine as claimed then the antibody of Hirth would bind. As far as the argument of "specifically binds" is concerned, this was addressed in the previous response, the specification does not define the phrase and as such the broadest interpretation is applied. In addition, applicants are directed to Roitt et al. (Immunology, third edition., Mosby, St. Louis, pages 6.4 and 6.5, 1993). Roitt teaches in the last sentence of the bridging paragraph of pages 6.4 and 6.5 that "when some of the determinants of an antigen, [for instance] A, are shared by another antigen, B, then a proportion of the antibodies directed to A will also react with B. This phenomenon is termed cross-reactivity." See Fig 6.8 on page 6.4. Furthermore, specificity is not equivocal to exclusivity. Roitt continues to state on page 6.5, column 2, second paragraph, "The specificity of a population of antibodies is not due to each antibody reacting exclusively with the induction antigen." The rejection is maintained because Hirth's antibody would be specific for SEQ ID NO:4.

The following are NEW GROUNDS of rejection

Claim Rejections - 35 USC § 112

9. Claims 122, 130, 138, 142 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 122 and 142 are indefinite for reciting “fully humanized” because it is unclear what the difference between “humanized” in claim 122 and 141 and the “fully humanized” antibody in claims 122 and 142 is.

b. Claims 130, 138 are indefinite for reciting “a 40 kd protein” from a lysate of C305cells and “the 40 kd protein” from lysate of non-transformed cells because are the two proteins the same or are they different?

10. Claims 103-122 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 103 has been amended to recite “generated against a polypeptide comprising at least about five non-phosphorylated amino acids”. Support for the limitation is said to come from claims 73-79, 82, 85, and 88 (see page 10 of response). The response has been carefully considered but is deemed not to be persuasive. The

Art Unit: 1642

original claims 73-79, 82, 85, and 88 do not support a polypeptide that has about five non-phosphorylated amino acids. The claims were directed to a polypeptide that comprised about 5 or 20 amino acids or 31-233 or cytosolic tail of SEQ ID NO:4. there is no support for eliminating the phosphorylated residue. Applicant is required to provide specific support for the claim limitation in the specification as originally filed or remove it from the claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 123, 132-142 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buday et al (The Journal of Biological Chemistry 269:9019-23, 1994), and further in view of Queen et al (US Patent 6,180,370, filed 6/95).

Art Unit: 1642

The claims recite an antibody that binds specifically to a polypeptide comprising a phosphotyrosine residue of at least 5, 20 amino acids, residues 31-233 of SEQ ID NO:4, cytosolic tail of SEQ ID NO:4 wherein the antibody is monoclonal, humanized or chimeric.

Buday et al teach a monoclonal antibody 4G10 that is an anti-phosphotyrosine antibody and the antibody binds to the p36 protein (see Figure 4A). Buday et al teach the protein p36 which is a 36 kDa protein that is phosphorylated and membrane bound and is associated with TCR (see abstract and page 9022). The specification discloses a 36 kDa polypeptide that is phosphorylated by ZAP-70 and that is associated with T cell receptors (see page 66 and 68 of specification). Because of the open language of the term "comprising" the claims are interpreted to mean the recited amino acid portions plus other amino acids which reads on the entire protein which would contain tyrosine residues that are phosphorylated. Since Buday teach a anti-phosphotyrosine antibody, the protein is phosphorylated, and as disclosed in the specification that the protein is phosphorylated, therefore the antibody of Buday et al would specifically bind to SEQ ID NO:4. Buday et al does not teach a humanized antibody. This deficiency is made up for in the teachings of Queen et al.

Queen et al teach humanized antibodies for detection of human antigens.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have humanized the antibody of Buday by the method of Queen et al.

Art Unit: 1642

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have humanized the antibody of Buday by the method of Queen et al because Buday et al teach the antigen is a human antigen and in view of Queen et al who teaches detection of human antigens with human antibodies to eliminate unwanted immunogenic responses, it would have been obvious to humanize the antibody of Buday for detection in humans.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

13. Claims 91-102 and 143 are in condition for allowance.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

Art Unit: 1642

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is ~~703-872-9306~~. 571 273 8300

Respectfully,

Larry R. Helms Ph.D.

571-272-0832


LARRY R. HELMS, PH.D
PRIMARY EXAMINER